Prophylaxis of Invasive Fungal Infections: A Review of the Use of Posaconazole

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Abstract: Invasive fungal infections (IFIs) cause significant morbidity, mortality, and increased cost of care in patients with hematological malignancies, prolonged (i.e. >7–10 days) treatment induced neutropenia, and other disease states causing underlying immunosuppression. One strategy often used to combat the development of invasive infections is the use of antifungal agents as prophylaxis in at risk patients. Posaconazole is an oral triazole with a useful spectrum of activity against many fungal pathogens of concern in patients at risk for the development of IFIs. Posaconazole is only available in oral formulation and therapeutic drug monitoring may provide value due to variable absorption and serum concentrations. Clinical efficacy and pharmacoeconomic data have demonstrated the utility of posaconazole in the treatment of oropharyngeal candidiasis and for prophylaxis in patients at risk for development of IFIs. Several organizations or expert groups involved in developing guidelines for the management of IFIs recommend posaconazole anti-fungal prophylaxis in patients with AML or MDS and chemotherapy induced neutropenia or significant GVHD. In addition, nonrandomized studies (largely of salvage therapy) and case series suggest that posaconazole may be effective as treatment for invasive aspergillosis, zygomycosis, and coccidiomycosis. Further, small case series or individual case reports suggest activity against other less commonly encountered filamentous fungi and Histoplasma.

Keywords: posaconazole, fungal prophylaxis, invasive fungal infections
Introduction

Invasive fungal infections (IFIs) cause significant morbidity, mortality, and increased cost of care in patients with hematological malignancies, prolonged (i.e. >7–10 days) treatment induced neutropenia, and other disease states or treatments resulting in immunosuppression.\(^{1,2}\) For example, patients who receive allogeneic hematopoietic stem cell transplant (HSCT) are more likely to develop invasive aspergillosis with an incremental cost of treatment estimated in 1998 at $86,635.\(^{2,3}\) Most concerning are the fatality rates associated with these difficult to treat infections which may range as high as 60% to 90% and complicate or delay further chemotherapy, thus compromising treatment of the underlying malignancy.\(^{4,5}\)

One strategy often used to combat the development of invasive infections involves the use of antifungal agents as prophylaxis in at risk patients. Robenshtok and colleagues evaluated the effect of antifungal prophylaxis on all-cause mortality in cancer patients after chemotherapy or HSCT.\(^{6}\) Prophylaxis reduced all-cause mortality, fungal-related mortality, and documented IFIs in patients who received allogeneic HSCTs (RR, 0.62; 95% CI, 0.45 to 0.85). They concluded, “antifungal prophylaxis should be administered to patients undergoing allogeneic HSCT, and should probably be administered to high-risk acute leukemia patients.” Supporting this conclusion are recent recommendations from the National Comprehensive Cancer Network and the German Society for Haematology and Oncology, and the Infectious Disease Society of America which all recommend antifungal prophylaxis as a means to prevent or reduce IFIs in immunosuppressed patients.\(^{7–9}\)

Clinicians must navigate a delicate balance between efficacy, safety, coverage spectrum, cost, and drug interaction profile when choosing suitable prophylaxis agents from the antifungal armamentarium. Fluconazole has long been used as a prophylaxis agent in patients with acute leukemia or myelodysplastic syndrome (MDS), but mortality benefit has not been well documented in this population and there is growing concern for the increase in pathogens less susceptible to fluconazole. Fortunately, the last decade saw the arrival of newer treatment options with expanded coverage spectrums. Voriconazole, posaconazole, and the echinocandins (anidulafungin, micafungin, and caspofungin) have increased coverage spectrums relative to fluconazole and are generally less toxic than amphotericin products. These new agents have allowed researchers and clinicians to explore the role these new agents play in the prophylaxis of IFIs. Of the newer agents, micafungin and posaconazole have obtained indications from the United States Food and Drug Administration (FDA) for the prophylaxis of IFIs and voriconazole, itraconazole, and amphotericin products are recommended by the National Comprehensive Cancer Network (NCCN) as antifungal options for prophylaxis.\(^{7,10,11}\) Of these, the NCCN recommends the most recent addition to the antifungal armamentarium, posaconazole, as the drug of choice for prophylaxis in neutropenic patients with AML and MDS and significant graft versus host disease (GVHD). This manuscript focuses on posaconazole and explores the rationale behind this recommendation for prophylaxis of IFIs. The use of posaconazole in the treatment of IFIs is also detailed.

Indications

Posaconazole (Noxafil, Schering-Plough Corp., Kenilworth, NJ USA) was approved by the FDA in September 2006 for prophylaxis of IFIs due to Aspergillus and Candida in patients older than 13 years of age at high risk of developing IFIs due to being severely immunocompromised, such as HSCT recipients with GVHD or those with hematologic malignancies with prolonged neutropenia from chemotherapy. The European Union followed a month later in October 2006, posaconazole received EU marketing approval for prophylaxis of IFIs in patients receiving remission-induction chemotherapy for acute myelogenous leukemia or myelodysplastic syndromes expected to result in prolonged neutropenia and HSCT recipients who are undergoing high-dose immunosuppressive therapy for GVHD.\(^{11}\) Indications for the treatment of oropharyngeal candidiasis (OPC) followed later.\(^{12}\) The prospective trials which were the basis for these indications will be described in the section “Clinical Studies”.

Mechanism of Action, In Vitro Activity, and Drug Interactions

Posaconazole is an oral broad-spectrum triazole with an extended side chain similar in chemical structure to itraconazole. It acts through inhibition of CYP51
which results in depletion of ergosterol, ultimately disturbing membrane function, replication, and can lead to cell death. Posaconazole has in vitro activity against Aspergillus spp. including Aspergillus fumigatus, Aspergillus flavus, and Aspergillus niger. Posaconazole also exhibited in vitro activity against Cryptococcus spp. and a wide variety of Candida spp. including Candida glabrata isolates with increased MIC values to fluconazole and fluconazole-resistant Candida krusei. Of note, posaconazole appears to be the only oral option for the treatment of zygomycetes. Reports of resistance to posaconazole remain rare, though reports of Aspergillus fumigatus and Candida albicans resistance exist in the literature. Resistance in both organisms is thought to be caused by point mutations in CYP51.

Absorption and Variability of Posaconazole Levels

Posaconazole concentrations have significant and unpredictable inter-patient variability. Posaconazole is not available in intravenous formulations and many patients find it difficult to take posaconazole four times daily with food because of underlying nausea, mucositis or other illness associated factors. The oral solution is cherry flavored and not unpleasant. Nonetheless, the lack of an intravenous form is a significant limitation of the drug in patients.

The variations in posaconazole concentrations relate to marked variability in absorption of the orally administered drug. There are many factors which affect the absorption of posaconazole. First, posaconazole exhibits saturable absorption-absorption is markedly enhanced when the drug is delivered in smaller divided doses. This means that despite the long elimination half-life (35 hours), serum concentration is significantly higher when the drug is delivered in multiple daily doses. In a study with healthy volunteers, the fractionation of an 800 mg/day dosage into a dose of 400 mg twice daily was shown to increase posaconazole exposure by nearly 100%. Further fractionation of the dose to 200 mg four times daily enhanced absorption by 220%.

The prandial state of the patients also greatly affects drug absorption. The absorption is greatly enhanced when the posaconazole is administered with food. For example, the absorption of posaconazole is increased 2.6 times when the oral suspension is administered with a low fat meal or a nutritional supplement. This is increased almost 4 times when the drug is given with a high fat meal (approximately 50 g fat). The timing of the dose in comparison with the meal is also important. For example optimal absorption was observed when the drug was taken during or within 20 minutes after a high fat meal.

This characteristic has been a significant limitation of posaconazoles utility in sick and hospitalized patients in whom poor appetite, gastrointestinal disturbance such as nausea, vomiting or diarrhea, mucositis and medical testing may cause the patient to have poor dietary intake. This may explain the observation that lower posaconazole levels are found in patient groups versus healthy volunteers. Significant inter-patient differences in levels have been observed. For example, in a study of neutropenic stem cell transplant recipients, variability in the reported pharmacokinetic parameters was as much as 68%. In that same study, it was noted that the serum level was dose related but not dose proportional. In a study of 98 patients with refractory febrile neutropenia or known invasive fungal infection, concentrations of posaconazole was 52% lower in allogeneic bone marrow transplant recipients than in patients without transplants. Finally, a recent study relevant to critically ill patients, has shown a decrease in levels obtained in persons in whom the drug was administered by nasogastric tube. The reason for this effect is not known.

Medications have also been shown to reduce the concentration of posaconazole. Many do this by impairing gastrointestinal absorption. For example, concomitant use of metoclopramide with posaconazole significantly reduced the concentration of posaconazole, presumably because enhanced GI transit reduced the GI mucosal exposure to the drug. Additionally, much like itraconazole, the absorption of posaconazole appears to be enhanced in an acidic gastritic milieu. Therefore, agents which temper gastric acidity impair the absorption of posaconazole.
at risk for invasive fungal infection are very often given proton pump inhibitors or other acid reducing medications in an effort to prevent gastrointestinal bleeding. Much like itraconazole, the administration of posaconazole with a low-pH drink such as ginger-ale enhanced absorption.24

Several other drugs are also noted to produce lower than expected drug concentrations due to induction of the metabolism via UDP glucuronidation. These drugs include rifabutin, phenytoin, efavirenz.12

Because of these factors which significantly reduce drug exposure, there has been concern that patients outside of the clinical trial environment would not be able to obtain sufficient posaconazole levels to prevent or treat infection. This was demonstrated in a real world assessment of clinical samples from a reference laboratory which was recently published.27 In this series, 70% of clinical samples were <0.7 µg/ml. This value is significant because it is the threshold concentration cited by the FDA below which patients at increased risk.28 Nearly 18% of clinical samples had levels below the threshold value which was associated with a greatly reduced response rate in salvage therapy for invasive aspergillosis and 16.3% had undetectable posaconazole levels.29

Relationship of serum concentration to efficacy
Posaconazole has concentration dependant efficacy both in animal models and in patients.29–31 In one trial of posaconazole as salvage therapy in patients with invasive aspergillosis, just over 20% of patients with an average plasma concentration of 0.13mg/L or less had a clinical response, while the clinical response was over 70% in patients who had an average steady state concentration of 1.25 mg/L.29

Two large studies, which will be described in greater detail in the “Clinical Studies” section, demonstrated substantially fewer breakthrough infections caused by Aspergillus species in patients receiving posaconazole prophylaxis when compared to patients receiving fluconazole or itraconazole.32,33 It is worth noting that, while the differences did not reach statistical significance, the posaconazole concentrations were two times lower in patients who developed an invasive fungal infection than in patients who did not. Statistical significance may have been difficult to demonstrate given the small number of patients who did develop infection during the study period.33

Given what has been learned about the variability of posaconazole absorption and serum concentrations this degree of efficacy in real groups of patients may be surprising. Some authors theorize that due to the drugs very large volume of distribution and long half-life, efficacy may be because the drug accumulates at the site of infection, but this has not been confirmed.20

Toxicity
The adverse effects of posaconazole are similar to those of other triazoles including drug interactions (particularly CYP3A inhibition), hepatotoxicity and, most commonly mild gastrointestinal disturbance such as nausea, vomiting or diarrhea. In a review of adverse effects seen in healthy volunteers the incidence of treatment associated adverse events reported with posaconazole was similar to that seen with placebo.34 Of 428 patients receiving posaconazole for refractory invasive fungal infections or febrile neutropenia, 38% of patients developed an adverse effect which may have been related to posaconazole use. However, only 8% developed a serious adverse effect.35 The most commonly reported adverse effects in patients was nausea reported in 8% and vomiting reported in 6%. A small number of patients developed corrected QT interval and/or QT interval prolongation. Elevated hepatic enzymes occurred in 2% but were frequently transitory and did not require drug discontinuation.35 The effect of posaconazole drug concentration on toxicity has not been demonstrated.

Recommendations for Therapeutic Posaconazole Monitoring
While the clinical experience with posaconazole is still limited, posaconazole appears to meet the cardinal indications for therapeutic drug monitoring, including wide inter-patient variation, concentration dependant efficacy, and an obtainable serum assay.27,36 Trough concentration monitoring may be considered towards the end of the first week of therapy, especially in patients with impaired GI mucosal absorption, impaired gastric acidity, or those patients receiving the BID or q day dosing schedule. A trough should be repeated in the setting of inadequate clinical response, after the addition of an interacting medication or with changes in dosage. The trough posaconazole
goal should be 0.5 to 1.5 $\mu$g/ml for patients being treated for invasive fungal infection. Some authors propose that the goal for prophylaxis may be lower than the level necessary for treatment and may be sufficient at the lower end of the range described above.\textsuperscript{37} Additionally, the FDA briefing document recommends a goal posaconazole average serum drug concentration of $>0.7 \mu$g/ml.\textsuperscript{28}

If low levels are found, the level may be improved by changing to 200 mg QID with a fatty meal and acidic beverage. However, some patients do not appear to respond to these changes and may continue to have low levels despite all efforts to enhance absorption.

**Clinical Studies**

As mentioned previously, the United States FDA indications for posaconazole include prophylaxis of invasive aspergillosis and candidiasis in high risk patients, and treatment of oropharyngeal candidiasis.\textsuperscript{12} Nonrandomized studies (largely of salvage therapy) and case series suggest that posaconazole may be effective as treatment for invasive aspergillosis, zygomycosis, and coccidiomycosis. Further, small case series or individual case reports suggest activity against other less commonly encountered filamentous fungi and \textit{Histoplasma}. The published clinical experience and the role of posaconazole for prophylaxis will be discussed. We also provide an overview of the clinical evidence for posaconazole in roles other than prophylaxis.

**Prophylaxis of invasive fungal infections in high risk patients**

Two large randomized controlled trials published in 2007 defined the role of posaconazole as prophylaxis for invasive fungal infections in high risk patients with hematological malignancies.\textsuperscript{32,33} Cornely and colleagues compared posaconazole to itraconazole or fluconazole in 602 patients with neutropenia resulting from chemotherapy for acute myelogenous leukemia or myelodysplastic syndrome.\textsuperscript{32} Posaconazole was dosed at 200 mg three times daily, and treatment continued during the period of neutropenia (or longer if complete remission was not achieved). Almost half of the patients experienced greater than 21 days of neutropenia. Invasive candidiasis was rare (1% or less), but invasive mold infections (largely aspergillosis) occurred in 2/304 (1%) of posaconazole patients versus 20/298 (7%) of fluconazole or itraconazole patients. Significantly, a mortality benefit was noted in patients receiving posaconazole prophylaxis. Serious adverse events likely related to the antifungal agent were more common in the posaconazole group; however, there was no difference (8%) in adverse events possibly or probably related to the antifungal leading to discontinuation.\textsuperscript{32}

Ullmann and colleagues conducted a similar trial randomizing 600 graft versus host disease (GVHD) patients to 112 days of posaconazole (200 mg three times a day) or fluconazole (400 mg daily). As GVHD is treated with immunosuppressive medications, these patients are at very high risk for IFIs. As in the previous trial, breakthrough invasive candidiasis was rare occurring in 8/600 patients during the treatment period. While the endpoint of invasive fungal infection was not significantly different between the two arms 16/301 (5.3%) posaconazole versus 27/299 (9.0%) fluconazole ($p = 0.07$), significantly fewer cases of invasive aspergillosis occurred on posaconazole 7/301 (2.3%) than on fluconazole 21/299 (7.0%) fluconazole. While no overall mortality benefit was observed, fewer deaths due to invasive fungal infection occurred in the posaconazole group.\textsuperscript{33}

These studies lead to the National Comprehensive Cancer Network (NCCN) and the Infectious Disease Society of America (IDSA) recommendations for posaconazole anti-fungal prophylaxis in patients with AML or MDS and chemotherapy induced neutropenia or significant GVHD.\textsuperscript{7,9} Cases have been reported, however, of breakthrough IFIs with \textit{Zygomycetes}, \textit{Aspergillus} and yeast (\textit{Tichosporon asahii} and \textit{Candida glabrata}) while on posaconazole prophylaxis.\textsuperscript{38–41} In some of these cases serum levels of posaconazole were within recommended ranges. Potential reasons for breakthrough include resistance, inadequate levels, and profound immunosuppression. It is also notable that no trial has assessed the efficacy of posaconazole in the first 75–100 days after stem cell transplant, a period during which fluconazole has been demonstrated to have a mortality benefit.\textsuperscript{42}

**Pharmacoeconomic analyses of prophylaxis**

Several recent pharmacoeconomic studies investigated the financial impact of posaconazole in the prophylaxis of IFIs.\textsuperscript{43–45} Utilizing efficacy results from the Cornely
trial, posaconazole is consistently predicted as a cost-effective prophylaxis alternative to fluconazole or itraconazole in patients with prolonged neutropenia.\textsuperscript{32} One study performed from the hospital perspective estimated patients initiated on posaconazole would have a 45% reduction in total treatment cost compared with patients initiated on fluconazole or itraconazole.\textsuperscript{33} The model was robust to all univariate changes in model variables, including medication cost, duration of therapy, and cost of treating invasive fungal infections. In all studies, utilizing posaconazole for the prophylaxis of IFIs decreased overall costs compared with fluconazole or itraconazole despite the higher medication acquisition cost.\textsuperscript{43–45} While pharmacy costs tended to be much higher, the cost-avoidance came from decreasing IFIs and their extraordinarily high associated treatment costs.

Further real-world pharmacoeconomic data regarding posaconazole is needed to validate the predictions of these models; however, these studies are often difficult to perform due to small sample size and large variability in treatment costs. While posaconazole dominates fluconazole or itraconazole in the prophylaxis of patients with prolonged neutropenia, further pharmacoeconomic data is also needed to investigate posaconazole’s financial value relative to other suitable prophylaxis options.

### Oropharyngeal candidasis

A randomized controlled trial demonstrated that posaconazole (200 mg day 1 followed by 100 mg daily to complete 2 weeks) was non-inferior to the same dose of fluconazole in AIDS patients with OPC.\textsuperscript{46} Because of low cost and excellent tolerability and efficacy, however, fluconazole remains the drug of choice for OPC when systemic therapy is employed. In the developed world, OPC refractory to fluconazole has become less common in the era of highly active antiretroviral therapy, but such cases can be difficult as recurrent courses of intravenous therapy with amphotericin products or echinocandins may be required. Skiest and colleagues demonstrated a response rate of 75% in HIV infected patients with azole refractory OPC or esophageal candidiasis even when typically fluconazole resistant species \textit{glabrata} or \textit{krusei} were present.\textsuperscript{47} The authors speculate that, given its long side chain, a greater number of mutations may be required for resistance to posaconazole as compared to voriconazole or fluconazole. It is notable that relapse occurred in almost three-quarters of patients within a month of completing therapy. Nonetheless, posaconazole remains a reasonable treatment option and avoids the need for intravenous therapy in patients with OPC refractory to fluconazole.

### Zygomycosis

While amphotericin products with or without surgery have long been the mainstay of therapy for zygomycosis, mortality remains high ranging from 10% to 100% depending on the host and site of disease.\textsuperscript{48} Given the \textit{in vitro} activity of posaconazole against \textit{Zygomycetes} (unique among currently FDA approved azoles), there has been considerable interest in defining the role of this drug in the treatment of zygomycosis. While an increasing incidence of zygomycosis has been noted, the disease remains uncommon and no randomized trial of treatment has been published.\textsuperscript{49} However, numerous case reports and one large case series have been reported describing the experience with posaconazole in patients with zygomycosis.\textsuperscript{50–61} Van Burik and colleagues published a retrospective report of the experience with posaconazole in patients with zygomycosis cases in the open label compassionate use trial of posaconazole as salvage therapy in invasive fungal infections.\textsuperscript{61} Ninety-one cases (69 proven, 22 probable) were included; 81 were refractory to primary therapy and 10 were intolerant. Surgical therapy was common 64/91, and over half of patients had a hematological malignancy. Dosing of 800 mg daily was employed. Complete or partial remission at 12 weeks occurred in 60% of patients and stable disease in 21%. Interestingly, success occurred in 72.7% of patients with brain lesions, suggesting good activity of posaconazole in the CNS.

In a single center review of 70 patients with a hematological malignancy and zygomycosis, posaconazole salvage therapy (administered to 15 patients) was associated with improved survival.\textsuperscript{62} Single case reports and small series suggest dramatic response after failure of amphotericin products, but given publication bias and the timing of other therapies (e.g. surgical resection) current data does not allow determination of whether or not posaconazole is superior, inferior, or equivalent to amphotericin products in the treatment of invasive zygomycosis.\textsuperscript{12,57,59,60} Nonetheless, the above data suggest posaconazole may be effective as
salvage therapy. In addition, it is an option in patients intolerant to amphotericin products. Further, as long durations of treatment are usually required, oral posaconazole is often used as continuation therapy as extended courses of intravenous amphotericin are impractical and usually result in toxicity. The efficacy of posaconazole in combination therapy for zygomycosis (e.g. with liposomal amphotericin) is currently unknown.

Aspergillosis
Based on clinical experience and a landmark clinical trial demonstrating superiority to amphotericin deoxycholate, voriconazole is first line therapy for the treatment of invasive aspergillosis (IA). No trial has compared posaconazole to voriconazole for the treatment of aspergillosis. Two case series with either historical or external controls examined the efficacy of posaconazole as salvage therapy for IA (or in those refractory to first line treatment). It should be noted that both trials predate the widespread use of voriconazole as primary therapy for IA. Walsh and colleagues compared response in 107 posaconazole recipients to 86 retrospectively selected control subjects in patients refractory to or intolerant of conventional therapy. A combined endpoint of global response as defined by an expert committee was met in 42% of posaconazole patients and 26% of control patients. In a separate trial, 3 IA salvage cohorts were retrospectively compared. Fifty-three patients were enrolled in the compassionate use posaconazole trial, 52 patients received high-dose lipid amphotericin B, and 38 received high-dose lipid amphotericin B and caspofungin. The response rate in the posaconazole cohort was 40% as compared to 8%–11% in the high-dose lipid amphotericin B cohorts. Posaconazole may be an option for IA in patients intolerant to voriconazole, cross-hepatoxicity in particular may not occur. Further, if amphotericin products are not an option posaconazole may be used as salvage therapy for voriconazole failures or if studies indicate voriconazole resistance and sensitivity to posaconazole.

Coccidiomycosis
Response to standard therapy (amphotericin products, itraconazole or fluconazole) in patients with coccidiomycosis is variable, and given excellent \textit{in vitro} activity three trials have explored the efficacy of posaconazole in patients with refractory coccidiomycosis. Anstead and colleagues describe 6 patients with clear progression receiving >40 days of treatment with active agents. Five patients improved within a month of receiving posaconazole. In another report of 20 highly pre-treated patients with non-meningeal disseminated or chronic pulmonary coccidiomycosis, 17/20 had a satisfactory response to a median of 173 days of treatment with posaconazole. One-third of patients who completed therapy relapsed, suggesting the need for extended or even indefinite treatment courses. Stevens and colleagues described a similar rate of success 11/15 (73%) in patients receiving a median of 306 days of primary treatment prior to salvage with posaconazole. While not first line therapy, the above data suggests posaconazole may be effective as salvage therapy for disseminated or chronic pulmonary coccidiomycosis.

Less common filamentous fungi, yeast, and histoplasma
Selecting the appropriate antifungal for less common filamentous fungi is challenging as controlled trials or large caser series are not available. Case reports of posaconazole as treatment for a variety of these infections are available. One case series and three single case reports describe the experience with posaconazole in patients with fusariosis. Raad and colleagues reviewed posaconazole treatment of 21 patients with hematological malignancy and fusariosis. A success rate of 48% was noted compared to a historical failure rate of 70% with amphotericin therapy; in GVHD patients or patients with refractory neutropenia success rates were much lower. It should be noted that no patients received voriconazole. One case report does, however, describe successful treatment of ocular fusariosis with posaconazole after failure to respond to voriconazole, perhaps related to higher ocular levels of posaconazole. Nonetheless, voriconazole is FDA approved for serious Fusarium infections, and most clinicians use voriconazole to treat fusariosis. Case reports describe successful salvage therapy with posaconazole for phaeohyphomycosis, Exophilia jeanselmei, Sceopspsiorium apiospermum, Scedosporium prolificans, Acremonium strictum, and chromoblastomycosis. Failure of posaconazole in
cases of Pseudoallescheria boydii, Apophysomyces elegans, Basidiomycete have been reported as well.77-83 In some of the successful cases, CNS infections were present. Particularly in that circumstance, if in vitro data suggests activity against the infecting mold, posaconazole may be a reasonable primary or salvage option for uncommon filamentous fungi.

Limited experience treating histoplasmosis is available. One case of disseminated histoplasmosis responded to posaconazole after failure of itraconazole, and a case series describes successful outcomes with posaconazole in 6 patients (5 disseminated, 1 pulmonary) failing standard therapy.84,85

Conclusions

Invasive fungal infections (IFIs) cause significant morbidity, mortality, and increased cost of care and antifungal prophylaxis is recommended as a means to prevent or reduce these infections in immunocompromised patients. Posaconazole, an oral broad-spectrum triazole, is a recent addition to the antifungal armamentarium available for the prophylaxis of IFIs. It displays an attractive spectrum of activity and safety profile compared with fluconazole or amphotericin B, respectively. The lack of intravenous formulation may be a barrier in some patients and therapeutic drug monitoring may provide value due to variable absorption and serum concentrations. Clinical and pharmacoeconomic data have demonstrated the utility of posaconazole for prophylaxis in patients at risk for development of IFIs and several organizations recommend posaconazole anti-fungal prophylaxis in patients with AML or MDS and chemotherapy induced neutropenia or significant GVHD.

Disclosures

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